UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,606	12/11/2003	Bei Chen	ABGENIX.058A	9342

20995 7590 02/26/2007

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
KIM, YUNSOO	
ART UNIT	**PAPER NUMBER**
1644	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	02/26/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 02/26/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

Office Action Summary	Application No.	Applicant(s)	
	10/734,606	CHEN ET AL.	
	Examiner	Art Unit	
	Yunsoo Kim	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38 and 40-48* is/are pending in the application.

4a) Of the above claim(s) *10-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,25-38 and 40-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/7/06 has been entered.

2. Claims 1-9, 25-38 and 40-48 are under consideration.

3. In view of Applicants' amendment to the claims, the following rejections remain.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-9, 25-38, 40, 42, 43, 45, 46 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over US2003/0138417(of record) A1 as is evidenced by the SYNAGIS product information sheet (of record) in view of U.S. Pat. No. 5,580,856 (of record).

The '417 publication teaches a stable liquid formulation comprising 50mg/ml IgG2 such as HuEP5C7, human monoclonal antibody to selectin ([0044, in particular]) in 50mM of Histidine, arginine ([0052, in particular]) and 125 mM NaCl (Example 11, [0107-0109], abstract, in particular) in the presence of polysorbate.

The claims 25-27, 29, 30, 43 and 45 drawn to "kit" are included in this rejection as the '417 publication teaches that many antibodies are in market are supplied with sterile water for injection such as Synagis ([0004], in particular). The Synagis product information sheet as evidenced includes antibody formulation is packaged as a kit.

The '417 publication does not teach solid formulation such as lyophilized (freeze-dried) formulation or use of arginine in concentration of 15mM-60mM.

However, the '856 patent teaches a process of drying (i.e. freeze drying or spray draying) is often employed to stabilize proteins in a lyophilized formulation for long-term storage in a broader temperature ranges (abstract, col. 1, lines 5-14, in particular) and use of arginine in concentration of about 0.5%-5% (col. 4, lines 30-50, in particular). Given the molecular weight of arginine being 174.2g/ml, 5% of arginine is equivalent to 28.9mM.

Therefore, it would have been obvious to one of the ordinary skill in the art at the time the invention was made to stabilize the liquid antibody formulation taught by the '417 publication with the lyophilization process as taught by the '856 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the '856 patent teaches that a lyophilized formulation improves the storage time in a broader temperature ranges (abstract, col. 1, lines 5-14, in particular).

From the teachings of references, it would have been obvious to one of ordinary skill in art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time of invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants' arguments filed on 9/11/06 have been fully considered but they were not persuasive.

Applicants traversed the rejection based on that reference does not teach the addition of arginine as currently amended and one of the ordinary skill in the art would not know if the stabilizer in a liquid formulation would work in the lyophilized formulation.

In light of the discussion above, it is general practice to dry proteins in presence of additives such as excipients, osmolytes or other stabilizer to improve storage time when protein is unstable in liquid formulation (col. 1-2 '856 patent, in particular). Thus, stabilizers in liquid formulation is generally suitable for lyophilized formulation and the combination of the references remains obvious.

6. Claims 1, 41, 44 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over US2003/0138417(of record) in view of U.S. Pat. No. 5,580,856 (of record) and U.S. Pat. No. 4,849,352 (of record).

The '417 publication and the '856 patent have been discussed, supra.

The '417 publication and the '856 patent do not teach immunospecific antibody fragments (e.g. $F(ab')_2$).

However, the '352 patent teaches a pharmaceutical composition comprising a polyclonal $F(ab')_2$ binds to any antigen, pepsin digested followed by ammonium sulfate precipitation (col. 3, lines 22-41, col. 2, lines 51-65). The '352 patent further teaches that the antibody fragments are quickly distributed in the body, filtered and excreted by the kidney. Toxin neutralization by antibody fragments and volume circulating are greater than IgG (col. 1-2 overlapping paragraph).

Therefore, it would have been obvious to one of the ordinary skill in the art at the time the invention was made to employ immunospecific fragments taught by the '352 patent in the lyophilzed antibody formulation as taught by the '417 publication and the '856 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the antibody fragment taught by the '352 patent produces more readily utilizable antibody. The '352 patent teaches intact IgG is too large to be excreted by kidney functions (col. 2, lines 22-50, in particular).

From the teachings of references, it would have been obvious to one of ordinary skill in art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time of invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants' arguments filed on 9/11/06 have been fully considered but they were not persuasive.

Applicants traversed the rejection based on that reference does not teach the addition of arginine as currently amended and one of the ordinary skill in the art would not know if the stabilizer in a liquid formulation would work in the lyophilized formulation.

In light of the discussion above, it is general practice to dry proteins in presence of additives such as excipients, osmolytes or other stabilizer to improve storage time when protein is unstable in liquid formulation (col. 1-2 '856 patent, in particular). Thus, stabilizers in liquid formulation is generally suitable for lyophilized formulation and the combination of the references remains obvious.

From the combined teachings of references, one of ordinary skill in art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary skill in the art at the time the invention was made, as evidenced by references, especially in the absence of evidence to the contrary.

7. The following new ground of rejection is necessitated by Applicants' amendment filed 9/11/06.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out this invention.

9. Claims 1-7, 25-28, 31-38, 40-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The specification and the claims as originally filed do not provide a clear support for the phrase "histidine and arginine" which deletes "in a concentration of from greater than 20mM to about 60mM" and reads on histidine at any concentration as in claim 1, " hisidine in solution... and arginine" which deletes "in a concentration of from greater than 20mM to about 60mM" and reads on histidine at any concentration as in claim 25, "histidine in a concentration less than 30mM" in claim 31 and "histidine is present in a concentration of from greater than 5mM to about 30mM" as in claim 38. The specification provides support for histidine concentration being 6-60mM. Amendments to the claim currently recite histidine at any concentration as in claims 1 and 25 and broaden the scope of the claimed invention. The particular concentration of histidine being 5-30mM or less that 30mM is not supported by the instant specification.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), y another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 1-9, 25-38, 40-48 are rejected under 35. U.S.C 102(a) or (e) as being anticipated by US 2002/0045571 A2.

The '571 publication teaches that the stable antibody formulation at about 80mg/ml containing about 50-100 mM histidine and arginine (claims 45-50, in particular) in presence of sugars, trehalose or polysorbate (claims 59-60, in particular) and this antibody formulation can be lyophilized ([0133-136], in particular).

The'571 publication further teaches that the buffer being histidine being16mM (examples 2-3, in particular), kit comprising proper diluents in separate container ([0153], in particular) and the antibody being human monoclonal antibody or antibody fragments as well as IgG2 ([0117-130], in particular).

Claims 4 and 34 which recite arginine concentration being about 15-60mM are included in this rejection because the reference antibody formulation teaches 50mM of buffer concentration in combination of salts and/or buffer as in claims 1 and 45. As the '571 publication also teaches the histidine concentration can be 16mM or 10mM as in examples 2-3, the rest of buffer and/or salt concentration would be in 34mM or 40mM which is encompassed by the claimed about 15-60mM of arginine.

Thus, the reference teachings anticipate the claimed invention.

12. No claims are allowable.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yunsoo Kim whose telephone number is 571-272-3176. The examiner can normally be reached on Monday thru Friday 8:30 - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yunsoo Kim
Patent Examiner
Technology Center 1600
February 12, 2007

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600